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10/803,653	03/18/2004	John McCafferty	05569.0004.DVUS12	8022

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/803,653	MCCAFFERTY ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/726,219.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/18/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendment to the claims received on February 21, 2007 amended claim 1.

The amendment to the claims received on October 26, 2007 amended claim 1.

The amendment to the claims filed on July 16, 2008 amended claim 1.

Claims 1-5 are currently pending and under consideration.

Priority

2. The present application claims status as a DIV of 09/726,219 filed November 28, 2000 (now U.S. Patent 6,806,079) which is a CON of 08/484,893 filed June 7, 1995 (now U.S. Patent 6,172,197) which is a CON of 07/971,857 filed January 8, 1993 (now U.S. Patent 5,969,108) which is 35 USC § 371 (national stage) application of PCT/GB92/00883 filed July 19, 1991. The present application also claims foreign priority to UK 9104744.9 filed March 6, 1991, UK 9110549.4 filed May 15, 1991, UK 9015198.6 filed July 10, 1990, UK 9022845.3 filed October 19, 1990, and UK 9024503.6 filed November 12, 1990.

Please note: several requests were made to change the Bib. Data Sheet to move PCT/GB92/00883 from the Foreign Applications section to the Continuing Data section of the Bib. Data Sheet. However, despite the information on the front of U.S. Patent 5,969,108 (i.e. national stage of PCT/GB92/00883), U.S. Patent 5,969,108 is not listed in the current USPTO records as a 35 USC § 371 (national stage) of PCT/GB92/00883. Applicants are requested to clarify whether U.S. Patent 5,969,108 is indeed a 35 USC § 371 (national stage) of PCT/GB92/00883.

3. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in the UK (i.e. UK 9104744.9 filed March 6, 1991, UK 9110549.4 filed May 15, 1991, UK 9015198.6 filed July 10, 1990, UK 9022845.3 filed October 19, 1990, and UK 9024503.6 filed November 12, 1990). A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the disclosure of foreign applications UK 9104744.9 filed March 6, 1991, UK 9015198.6 filed July 10, 1990, UK 9022845.3 filed October 19, 1990, and UK 9024503.6 filed November 12, 1990 fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. UK 9104744.9 filed March 6, 1991 (disclose phagemid and helper phage, but not contents of phagemid), UK 9015198.6 filed July 10, 1990 (disclose coat protein partially derived from the helper phage and partly from the phage Ab-gene III construct at page 21), UK 9022845.3 filed October 19, 1990 (helper phage and phagemid not disclosed), and UK 9024503.6 filed November 12, 1990 (disclose helper phage at page 25; do not disclose phagemid or contents of phagemid) fail to disclose a phagemid wherein the only nucleotide sequences derived from filamentous bacteriophage are an origin of replication and a gene III capsid protein (present claim 1). Application UK 9110549.4 filed May 15, 1991 disclosed the pHEN1 vector (i.e. a phagemid wherein the only nucleotide sequences derived from filamentous bacteriophage are an origin of replication and a gene III capsid protein). Therefore, the priority date for the presently claimed invention is May 15, 1991 (i.e. filing date of UK 9110549.4).

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on July 18, 2008 is being considered by the examiner.

Invention as Claimed

5. A method for producing a binding molecule specific for a particular target, which method comprises the steps of: (a) producing a population of filamentous bacteriophage particles displaying at their surface a population of binding molecules having a range of binding specificities, wherein each binding molecule in the population of binding molecules has a binding domain able to bind a target and wherein each filamentous bacteriophage particle contains a phagemid genome further comprising nucleic acid with a nucleotide sequence encoding the binding molecule which is displayed at the particle surface, wherein the only nucleotide sequences derived from filamentous bacteriophage in the phagemid genome are an origin of replication and a nucleotide sequence encoding a gene III capsid protein and wherein a helper phage, or a plasmid expressing complementing phage genes, is used to package said phagemid genome within each filamentous bacteriophage particle; (b) selecting for a filamentous bacteriophage particle displaying a binding molecule with a desired specificity by contacting the population of filamentous bacteriophage particles with a target so that individual binding molecules displayed on filamentous bacteriophage particles with the desired specificity bind to said target and variations thereof.

Withdrawn Objections

6. The objection of claims 1-5 regarding redundancy of claim language is withdrawn in view of the claim amendments received on July 16, 2008.

Maintained Rejections

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

8. Claims 1-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Ladner et al. U.S. Patent 5,223,409 (effective filing date of September 2, 1988) alone or as evidenced by the Promega Technical Bulletins for pGEM®-3Zf(-) and pGEM®-3Zf(+) and/or the Stratagene Instruction Manual for pBluescript® II phagemid vectors regarding the nucleic acids derived from filamentous bacteriophage contained within the vectors.

For present claim 1, Ladner et al. teach methods of displaying binding proteins on the surface of filamentous bacteriophage via nucleic acid sequences including gIII and screening for target molecule binding wherein phagemids and helper phage may be utilized (please refer to entire document particularly abstract; columns 1, 4-12, 15-105; Examples I-XVI; claims 1-66). Ladner et al. teach phagemid vectors particularly phagemid vectors pBluescript® K/S and pGEM®-3Zf (i.e. only ori from filamentous bacteriophage; please refer to column 76; lines 55-67; column 77, lines 1-4; column 106) wherein the construct comprising gIII-binding domain would be inserted into the multiple cloning site for phage display (i.e. plasmid would then contain only ori and gIII of filamentous bacteriophage; please refer to columns 53-59, section IV.B)

For present claim 2, Ladner et al. teach separating bacteriophage expressing binding proteins from the target molecules (please refer to entire document particularly columns 10-12, 93-98).

For present claim 3, Ladner et al. teach recovering separated bacteriophage (please refer to entire document particularly columns 10-12, 98-99).

For present claim 4, Ladner et al. teach expressing the binding protein in another expression system including bacterial cells, spores, and artificial methods, etc. (please refer to entire document particularly columns 8, 10, 50-77).

For present claim 5, Ladner et al. teach utilizing the methods to express antibodies including the Fc portion (please refer to entire document particularly columns 15-16).

Therefore, the presently claimed invention is anticipated by the teachings of Ladner et al.

Arguments and Response

9. Applicants' arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Ladner et al. alone or as evidenced by the Promega Technical Bulletins for pGEM®-3Zf(-) and pGEM®-3Zf(+) and/or the Stratagene Instruction Manual for pBluescript® II phagemid vectors regarding the nucleic acids derived from filamentous bacteriophage contained within the vectors for claims 1-5 were considered but are not persuasive for the following reasons.

Applicants contend that Ladner et al. stated a concern regarding that if a helper phage is used there will be recombination between different DNA encoding displayed molecules and thus the genotype/phenotype connection may be lost; Ladner et al. did not actually use the pBluescript® II in the methods so the disclosure can not be relied upon; the pGEM®-3Zf(-) and pGEM®-3Zf(+) was utilized by Ladner et al. as starting material for a vector employing the gene VIII coat protein (i.e. not the gene III protein as presently claimed); and Ladner et al. teach utilizing the signal peptide of gene VIII wherein applicants assert that the gene VIII signal

peptide is a nucleotide sequence derived form filamentous bacteriophage that is other than an ori and a gene III (i.e. only bacteriophage sequences in phagemid vector as presently claimed).

Applicants' arguments are not convincing since the teachings of Ladner et al. anticipate the method of the instant claims. Ladner et al. teach pBluescript® II and pGEM®-3Zf as art recognized phagemid vectors that can be utilized for phage display (see column 76-77 and 106). While pBluescript® II may not be a preferred embodiment for the specific method of Ladner et al. (i.e. directed evolution), pBluescript® II is part of the disclosure of Ladner et al. which is available for all that it fairly discloses to one of ordinary skill in the art (see MPEP § 2123; *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983); *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). In addition, Ladner et al. specifically state that while certain phagemids are not preferred for their purposes (i.e. controlling mutations via random mutagenesis of a limited number of predetermined codons; please refer to column 1, lines 40-52) because coinfections could lead to genetic recombination (i.e. non-controlled mutation), phagemids are suitable for developing a gene that causes a binding domain to appear on the surface of phage-like genetic packages (please refer to the paragraph spanning columns 76 and 77). Moreover, Ladner et al. teach that both gene III and gene VIII can be utilized for phage display interchangeably (see columns 51, 54-58) and the signal sequence is part of gene III (i.e. required for protein transport and viral assembly) or may be from a different source including bacterial phoA or bla genes (see the abstract; columns 9-10, 12, 23, 51-52).

It is also noted that at page 53 of the present specification, applicants state that gene III comprises a signal sequence. Page 53 reads: "The protein encoded by gene III has several domains (Pratt, D., et al., 1969 Virology 39:42-53., Grant, R.A., et al., 1981, J. Biol. Chem. 256:

539- 546 and Armstrong, J., et al., FEBS Lett. 135: 167- 172 1981.) including: (i) a signal sequence that directs the protein to the cell membrane and which is then cleaved off; (ii) a domain that anchors the mature protein into the bacterial cell membrane (and also the phage coat); and (iii) a domain that specifically binds to the phage receptor, the F-pilus of the host bacterium".

10. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Bass et al. U.S. Patent 5,688,666 (effective filing date of December 3, 1990; provided in IDS submitted March 18, 2004).

For present claim 1, Bass et al. teach methods for selecting novel proteins (i.e. growth hormone variants) having altered binding properties comprising producing a library (i.e. population) of filamentous bacteriophage (i.e. M13) surface displaying a library (i.e. population) of growth hormone (GH) variants or other mammalian proteins including antibodies (i.e. binding molecules having a range of binding specificities) wherein each filamentous bacteriophage contains a phagemid comprising nucleic acid encoding the GH variants and only nucleic acid sequences derived from filamentous bacteriophage consisting of ori (i.e. f1 ori) and gene III wherein a helper phage is utilized to package the phagemid, contacting the filamentous bacteriophage surface displaying the GH variants with ligands/targets, and selecting for binding (please refer to the entire specification particularly the abstract; Figures 1, 3, 5-9; column 4, lines 64-67; columns 5-17).

For present claim 2, Bass et al. teach separation of bound phage from the ligands/targets (i.e. dissociation; please refer to the entire specification particularly column 17, lines 35-54).

For present claim 3, Bass et al. teach recovering phage with the desired binding specificity (please refer to the entire specification particularly column 5, method step g, lines 19-20; column 17, lines 35-54).

For present claim 5, Bass et al. teach antibodies (i.e. Fc tail; please refer to the entire specification particularly column 5, lines 40-67; column 10, lines 5-50).

Therefore, the presently claimed invention is anticipated by the teachings of Bass et al.

Arguments and Response

11. Applicants' arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Bass et al. for claims 1-3 and 5 were considered but are not persuasive for the following reasons.

Applicants contend that Bass et al. has an effective filing date of December 3, 1990 regarding phage display.

Applicants' arguments are not convincing since the teachings of Bass et al. anticipate the method of the instant claims. Bass et al. has an effective filing date of December 3, 1990 as asserted by applicants. The presently claimed invention has a priority date of May 15, 1991 (i.e. filing date of UK 9110549.4). Therefore, Bass et al. is prior art under 35 USC 102(e).

Claim Rejections - 35 USC § 103

12. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bass et al. U.S. Patent 5,688,666 (effective filing date of December 3, 1990; provided in IDS submitted March 18, 2004) and Cunningham et al. U.S. Patent 5,534,617 (effective filing date of October 28, 1988).

For present claim 1, Bass et al. teach methods for selecting novel proteins (i.e. growth hormone variants) having altered binding properties comprising producing a library (i.e. population) of filamentous bacteriophage (i.e. M13) surface displaying a library (i.e. population) of growth hormone (GH) variants or other mammalian proteins including antibodies (i.e. binding molecules having a range of binding specificities) wherein each filamentous bacteriophage contains a phagemid comprising nucleic acid encoding the GH variants and only nucleic acid sequences derived from filamentous bacteriophage consisting of ori (i.e. f1 ori) and gene III wherein a helper phage is utilized to package the phagemid, contacting the filamentous bacteriophage surface displaying the GH variants with ligands/targets, and selecting for binding (please refer to the entire specification particularly the abstract; Figures 1, 3, 5-9; column 4, lines 64-67; columns 5-17).

For present claim 2, Bass et al. teach separation of bound phage from the ligands/targets (i.e. dissociation; please refer to the entire specification particularly column 17, lines 35-54).

For present claim 3, Bass et al. teach recovering phage with the desired binding specificity (please refer to the entire specification particularly column 5, method step g, lines 19-20; column 17, lines 35-54).

For present claim 5, Bass et al. teach antibodies (i.e. Fc tail; please refer to the entire specification particularly column 5, lines 40-67; column 10, lines 5-50).

However, Bass et al. does not teach recombinantly expressing the binding molecule separate from the filamentous bacteriophage particles.

For present claim 4, Cunningham et al. teach methods of phage displaying hGH variants via phagemid and helper phage wherein the hGH variants are screened and selected for binding

to ligands/targets wherein the recovered hGH variants can be cloned and expressed in non-phage (i.e. non-phagemid) expression vectors (please refer to the entire specification particularly columns 5 and 12-20 especially column 13, lines 51-64; Example II).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of phage displaying mammalian proteins taught by Bass et al. with the further expression of the mammalian proteins via an expression vector as taught by Cunningham et al.

One having ordinary skill in the art would have been motivated to do this because Cunningham et al. teach that an expression vector can be utilized for amplification (i.e. production of the selected protein in higher quantities; please refer to column 13, lines 51-64).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of phage displaying mammalian proteins taught by Bass et al. with the further expression of the mammalian proteins via an expression vector as taught by Cunningham et al. because of the disclosure by Cunningham et al. utilizing expression vectors to express proteins (please refer to column 4, lines 13-15; column 8, lines 45-67; columns 9-10; column 13, lines 51-64).

Therefore, the modification of the method of phage displaying mammalian proteins taught by Bass et al. with the further expression of the mammalian proteins via an expression vector as taught by Cunningham et al. render the instant claims *prima facie* obvious.

Arguments and Response

13. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Bass et al. and Cunningham et al. for claims 1-5 were considered but are not persuasive for the following reasons.

Applicants contend that Bass et al. has an effective filing date of December 3, 1990 regarding phage display.

Applicants' arguments are not convincing since the teachings of Bass et al. and Cunningham et al. render the method of the instant claims *prima facie* obvious. Bass et al. has an effective filing date of December 3, 1990 as asserted by applicants. The presently claimed invention has a priority date of May 15, 1991 (i.e. filing date of UK 9110549.4). Therefore, Bass et al. is prior art under 35 USC 102(e).

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

October 31, 2008